

### Remarks

Claims 2-6 and 74-78 are pending in this application. Claims 3-4 and 75-76 are amended to correct typographical errors in the structures. Support for the amendments can be found, for example, claims 3-4 as originally filed and on page 16, lines 8-12 of the specification. No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-4 of the Office Action, the claims are rejected under 35 U.S.C. § 103, as allegedly obvious over Jeffery *et al.*, *J. Chem. Soc., Perkin Trans.*, 1: 2583-9 (1996) ("Jeffery"). Applicants respectfully traverse this rejection.

It appears that the rejection is premised upon the examiner's allegation that Jeffery teaches the claimed compounds, in particular, "stereoisomers of hydroxylated derivative of sibutramine." (Office Action, page 2). In this regard, the Examiner points to compound 5a on page 2583, last compound in column 1 on page 2587, and last compound in column 1 on page 2587 of Jeffery. Applicants respectfully disagree.

First, Applicants respectfully submit that the Examiner's allegation that any stereomerically pure compounds are disclosed in Jeffery is simply incorrect. Compound 5a on page 2583 of Jeffery, as repetitively pointed out by Applicants, is not stereomerically pure, as the Examiner appears to suggest. As Applicants have pointed out, Compound 5a merely shows cis/trans isomerism of the groups attached to carbon atoms at 5- and 7-positions in relation to the cyclobutyl ring, but it does not show a stereomerically pure compound. Furthermore, Compound 5a (7-hydroxy derivatives of sibutramine), although showing "positional denotation" of certain chemical bonds, does not even show any "positional denotation" of any of the chemical bonds connected to chiral carbon atoms, *i.e.*, carbon atoms at 2- and 4-positions. Thus, Jeffery is completely silent about the stereoisomerism of Compound 5a.

Moreover, Applicants respectfully point out that the last compound in column 1 on page 2587 is also not stereomerically pure. Indeed, Jeffery clearly discloses that the compound referred to by the Examiner is a mixture of diastereomers. (See Jeffery, page 2587, right side column). Notably, no attempts

were made in Jeffery to separate out those diastereomers, nor is there any suggestion regarding desirability of such separation. Therefore, contrary to what the Examiner alleges, the last compound disclosed in column 1 on page 2587 is not stereomerically pure.

Finally, the last compound in column 1 on page 2588 is again not stereomerically pure. As a close reading of the portion of Jeffery referred to by the Examiner would make it clear, that portion discloses a synthesis of a trans-isomer of 3-(1-amino-3-methylbutyl)-3-(4-chlorophenyl)cyclobutan-r-1-ol, *i.e.*, Compound 5b disclosed on page 2585 of Jeffery.<sup>1</sup> There is no disclosure or suggestion whatsoever of any stereomerically pure compound in that portion, or other portions of Jeffery. Therefore, as Jeffery does not teach or suggest any stereomerically pure compounds, Applicants respectfully submit that the rejection of the claims should be withdrawn for this reason alone.

In addition, the claims are further not obvious over Jeffery because Jeffery actively teaches away from the claimed invention. This is because Jeffery, by providing that the pharmacological activity of sibutramine is “mediated *predominantly* by” two demethylated amines of sibutramine (Compounds 2 and 3), which are not recited by the pending claims, would have discouraged those skilled in the art from obtaining and investigating the claimed compounds. (*See* Jeffery, page 2583, left side column). For this additional reason, Applicants respectfully request that the rejection of the claims 35 U.S.C. § 103 be withdrawn.

### **Conclusion**

In sum, Applicants respectfully submit that: 1) Jeffery and Fang fail to establish a *prima facie* case of obviousness; and 2) presumption of obviousness, if any, should be rebutted in view of the teaching away by Jeffery’s disclosure. For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that the rejection of the claims be withdrawn.

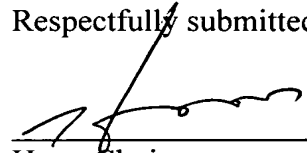
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<sup>1</sup> The cis-isomer of the same compound is Compound 5a, referred to by the Examiner.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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